

Incorporation of Sparsity Information in Large-scale Multiple Two-sample t Tests

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Abstract

Large-scale multiple two-sample *Student's t* testing problems often arise from the statistical analysis of scientific data. To detect components with different values between two mean vectors, a well-known procedure is to apply the Benjamini and Hochberg (B-H) method and two-sample *Student's t* statistics to control the false discovery rate (FDR). In many applications, mean vectors are expected to be sparse or asymptotically sparse. When dealing with such type of data, *can we gain more power than the standard procedure such as the B-H method with Student's t statistics while keeping the FDR under control?* The answer is positive. By exploiting the possible sparsity information in mean vectors, we present an uncorrelated screening-based (US) FDR control procedure, which is shown to be more powerful than the B-H method. The US testing procedure depends on a novel construction of screening statistics, which are asymptotically uncorrelated with two-sample *Student's t* statistics. The US testing procedure is different from some existing *testing following screening* methods (Reiner, et al., 2007; Yekutieli, 2008) in which independence between screening and testing is crucial to control the FDR, while the independence often requires additional data or splitting of samples. An inappropriate splitting of samples may result in a loss rather than an improvement of statistical power. Instead, the uncorrelated screening US is based on the original

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data and does not need to split the samples. Theoretical results show that the US testing procedure controls the desired FDR asymptotically. Numerical studies are conducted and indicate that the proposed procedure works quite well.

Keywords: false discovery rate, *Student's t* test, testing following screening, uncorrelated screening.

1 Introduction

Modern statistical analysis of high-dimensional data often involves multiple two-sample hypothesis tests

$$H_{i0} : \mu_{i,1} = \mu_{i,2} \quad \text{versus} \quad H_{i1} : \mu_{i,1} \neq \mu_{i,2}, \quad 1 \leq i \leq m,$$

where $\boldsymbol{\mu}_1 = (\mu_{1,1}, \dots, \mu_{m,1})$ and $\boldsymbol{\mu}_2 = (\mu_{1,2}, \dots, \mu_{m,2})$ are two population mean vectors and m usually can be tens of thousands. Ever since the seminal work of Benjamini and Hochberg (1995), the false discovery rate (FDR) control is becoming more and more desirable in large-scale multiple testing problems. The concept of FDR control not only provides an easily accessible measure on the overall type I error but also allows higher statistical power than the conservative family-wise error rate control. Let p_1, \dots, p_m be p-values calculated from two-sample *Student's* statistics for H_{10}, \dots, H_{m0} , respectively. The well known Benjamini and Hochberg (B-H) method rejects H_{j0} if $p_j \leq p_{(\hat{k})}$, where

$$\hat{k} = \max\{0 \leq k \leq m : p_{(k)} \leq \alpha k/m\}$$

and $p_{(1)} < \dots < p_{(m)}$ are the order p-values. Benjamini and Hochberg (1995) prove that their procedure controls the FDR at level α if p_1, \dots, p_m are independent. After their seminal work, there are a huge amount of literature on the FDR control under various settings; see Benjamini and Yekutieli (2001), Efron (2004,2007), Storey (2003), Storey, et al. (2004), Ferreira and Zwinderman (2006), Wu (2008), Sun and Cai (2009), Cai, et al. (2011) and so on.

In many applications, the mean vectors $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$ are expected to be sparse or asymptotically sparse. For example, in genetics, a quantitative trait could be controlled by a few major genes and many polygenes, and it is typically assumed that the polygenes have vanishingly small effects. In genome-wide association studies (GWAS), by marginal regressions, Fan, et al. (2012) convert GWAS into large-scale multiple testing $H_{i0} : \mu_i = 0$,

$1 \leq i \leq m$, for a mean vector (μ_1, \dots, μ_m) of m -dimensional normal random vector, where μ_i denotes the correlation coefficient between the i -th SNPs and a response such as genetic traits or disease status. It is reasonable to assume that only a few SNPs contribute to the response so that (μ_1, \dots, μ_m) is expected to be asymptotically sparse. In the estimation of high-dimensional mean vectors and the context of signal detections, mean vectors are also often assumed to be sparse; see Abramovich, et al. (2006), Cai and Jeng (2011) and Donoho and Jin (2004).

When $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$ are (asymptotically) sparse, *can we gain more power than standard procedures such as the B-H method with Student's t statistics while keeping the FDR under control?* The answer is trivially positive if the union support $\mathcal{S}_1 \cup \mathcal{S}_2$ of $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$ is known and small, where $\mathcal{S}_j = \{i : \mu_{i,j} \neq 0\}$, $j = 1, 2$. Actually, the support of $\boldsymbol{\mu}_1 - \boldsymbol{\mu}_2$ is contained in $\mathcal{S}_1 \cup \mathcal{S}_2$. Applying the B-H method to those components with indices in $\mathcal{S}_1 \cup \mathcal{S}_2$ will significantly improve the statistical power. The union support $\mathcal{S}_1 \cup \mathcal{S}_2$ is of course unknown and can even be as large as $\{1, 2, \dots, m\}$ if $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$ are asymptotically sparse. One may screen the mean vectors to obtain an estimate for the union support in the first stage and test the set of identified hypotheses while controlling the FDR in the second stage. This is known as *testing following screening* method which has been used in other multiple testing problems; see Zehetmayer, et al. (2005), Reiner, et al. (2007) and Yekutieli (2008). For such method, independence between screening in the first stage and hypothesis testing in the second stage is crucial to control the FDR. If independence is absent, by a simulation study, Reiner, et al. (2007) show that when hypotheses are screened by 1-way ANOVA F tests, the B-H procedure is unable to control the FDR in the second step as p-values no longer remain Uniform $(0, 1)$. In Section 4, we will further state some simulation results and show that it is impossible to control the FDR with the B-H method and some seemingly natural screening statistics. The independence between screening and hypothesis testing often requires additional data or splitting of samples. In the latter approach, it is difficult to determine the reasonable fractions of samples in two stages and the result may be unstable in real data applications. Moreover, a simulation study in Section 4 indicates that an inappropriate splitting of samples may result in a loss of statistical power.

In this paper, we present an uncorrelated screening-based (US) testing procedure for the FDR control, by a novel construction of screening statistics which are asymptotically uncorrelated with two-sample *Student's t* statistics. Instead of the independence assump-

tion between screening and testing, we show that in the US procedure, an asymptotic zero correlation is sufficient for the FDR control. The US procedure does not require any other samples or splitting of samples. It is demonstrated that the proposed US procedure is more powerful than the classical B-H method while keeping the FDR controlled at the desired level. Particularly, we prove that the range of signal sizes, in which the power of the US procedure converges to one, is wider than that of the B-H method, by exploiting the possible sparsity information in mean vectors. The asymptotic sparsity assumption for the power results in Section 3.2 is quite weak. It allows m^γ , $0 < \gamma < 1$, components of mean vectors that can be arbitrarily large. The remaining components can be of the order of $\sqrt{\log m/n}$, which may still be moderately large for ultra-high dimensional settings, for example, $\log m \geq cn$ for some $c > 0$. On the unfavorable case that $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$ are non-sparse at all, the US procedure will still be at least as powerful as the B-H method. That is, the US procedure does not really require the sparsity assumption on $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$. But if they share asymptotic sparsity, then US procedure can incorporate this information and improves statistical power.

We shall note that the exact null distributions of two-sample *Student's t* statistics are typically unknown. The US procedure does not require the true null distributions. Instead, our results show that it is robust to the asymptotic null distributions under some moment conditions. Moreover, our results allow K -dependence between the components of populations.

The remainder of this paper is organized as follows. In Section 2, we introduce the US testing procedure. Section 3 gives theoretical results on the FDR and FDP control. Theoretical comparisons between the US procedure and the B-H method are also given. The simulation study is presented in Section 4 and a discussion on several possible extensions is given in Section 5. The proofs of main results are postponed to Section 6. Throughout, we let C and $C_{(\cdot)}$ denote positive constants which may be different in each place. For two sequences of real numbers $\{a_m\}$ and $\{b_m\}$, write $a_m = O(b_m)$ if there exists a constant C such that $|a_m| \leq C|b_m|$ holds for all sufficiently large m , and write $a_m = o(b_m)$ if $\lim_{m \rightarrow \infty} a_m/b_m = 0$. For a set $\mathbf{A} \subset \{1, 2, \dots, m\}$, $|\mathbf{A}|$ denotes its cardinality.

2 Uncorrelated screening-based FDR control procedure

In this section, we introduce the US testing procedure. Let $\mathcal{X}_1 := \{\mathbf{X}_{k,1}, 1 \leq k \leq n_1\}$ and $\mathcal{X}_2 := \{\mathbf{X}_{k,2}, 1 \leq k \leq n_2\}$ be i.i.d. random samples from \mathbf{X}_1 and \mathbf{X}_2 , respectively, where $\boldsymbol{\mu}_1 = \mathbb{E}\mathbf{X}_1$ and $\boldsymbol{\mu}_2 = \mathbb{E}\mathbf{X}_2$. Assume that \mathcal{X}_1 and \mathcal{X}_2 are independent. Set

$$\mathbf{X}_{k,1} = (X_{k,1,1}, \dots, X_{k,m,1}) \quad \text{and} \quad \mathbf{X}_{k,2} = (X_{k,1,2}, \dots, X_{k,m,2}).$$

Let $\mathbf{X}_j = (X_{1,j}, \dots, X_{m,j})$, $j = 1, 2$. The variances $\sigma_{i,1}^2 = \text{Var}(X_{i,1})$ and $\sigma_{i,2}^2 = \text{Var}(X_{i,2})$, $1 \leq i \leq m$.

Case I, equal variances $\sigma_{i,1}^2 = \sigma_{i,2}^2$, $1 \leq i \leq m$. We define two-sample *Student's t* statistic for H_{i0} by

$$T_i = \sqrt{\frac{n_1 n_2}{(n_1 + n_2) \hat{\sigma}_{i,pool}^2}} (\bar{X}_{i,1} - \bar{X}_{i,2}),$$

where

$$\bar{X}_{i,j} = \frac{1}{n_j} \sum_{k=1}^{n_j} X_{k,i,j} \quad \text{and} \quad \hat{\sigma}_{i,pool}^2 = \frac{1}{n_1 + n_2 - 2} \sum_{j=1}^2 \sum_{k=1}^{n_j} (X_{k,i,j} - \bar{X}_{i,j})^2$$

for $j = 1, 2$. The key step in the US testing procedure is the construction of an uncorrelated screening statistic which can screen out nonzero components. In equal variances case, the US procedure uses

$$S_i = \sqrt{\frac{n_1^2}{(n_1 + n_2) \hat{\sigma}_{i,pool}^2}} (\bar{X}_{i,1} + \frac{n_2}{n_1} \bar{X}_{i,2})$$

as a screening statistic.

Case II, variances $\sigma_{i,1}^2$ and $\sigma_{i,2}^2$ are not necessary equal. In this case, we define two-sample *Student's t* statistic

$$T_i = \frac{\bar{X}_{i,1} - \bar{X}_{i,2}}{\sqrt{\hat{\sigma}_{i,1}^2/n_1 + \hat{\sigma}_{i,2}^2/n_2}}, \quad \text{where} \quad \hat{\sigma}_{i,j}^2 = \frac{1}{n_j - 1} \sum_{k=1}^{n_j} (X_{k,i,j} - \bar{X}_{i,j})^2$$

for $j = 1, 2$. The US procedure uses

$$S_i = \sqrt{\frac{n_1}{\hat{\sigma}_{i,1}^2 (1 + \frac{n_2 \hat{\sigma}_{i,1}^2}{n_1 \hat{\sigma}_{i,2}^2})}} (\bar{X}_{i,1} + \frac{n_2 \hat{\sigma}_{i,1}^2}{n_1 \hat{\sigma}_{i,2}^2} \bar{X}_{i,2})$$

as a screening statistic.

The construction of screening statistic is quite straightforward, but the idea can be extended to many other two-sample testing problems. Note that S_i is asymptotically equivalent to

$$S_{0i} := \sqrt{\frac{n_1}{\sigma_{i,1}^2(1 + n_2\sigma_{i,1}^2/(n_1\sigma_{i,2}^2))}}(\bar{X}_{i,1} + \frac{n_2\sigma_{i,1}^2}{n_1\sigma_{i,2}^2}\bar{X}_{i,2}),$$

which is uncorrelated with $\bar{X}_{i,1} - \bar{X}_{i,2}$. Note that

$$\mathbb{E}S_{0i} = \sqrt{\frac{n_1}{\sigma_{i,1}^2(1 + n_2\sigma_{i,1}^2/(n_1\sigma_{i,2}^2))}}(\mu_{i,1} + \frac{n_2\sigma_{i,1}^2}{n_1\sigma_{i,2}^2}\mu_{i,2}).$$

Hence, S_i can filter out zero components while keeping nonzero components. If the signs of $\mu_{i,1}$ and $\mu_{i,2}$ are opposite, then $\mathbb{E}S_{0i}$ can be small. However, we do not need to care about this case. It will always be easier for T_i to detect components with $\mu_{i,1}\mu_{i,2} < 0$ than those with the same signal sizes but $\mu_{i,1}\mu_{i,2} > 0$, because signals in the first case are stronger than signals in the latter case in terms of $\mu_{i,1} - \mu_{i,2}$. For the components which haven't been selected by S_i , a separate multiple testing will be applied on them.

We use $\Psi(t)$, the *Student's t* distribution with $n_1 + n_2 - 2$ degrees of freedom, as an asymptotic null distribution for T_i . It is clearly that other distributions such as the normal distribution or bootstrap empirical null distribution can be used. Suppose that we threshold $|S_i|$ at level λ and divide H_{i0} , $1 \leq i \leq m$, into two families $\{H_{i0} : |S_i| \geq \lambda\}$ and $\{H_{i0} : |S_i| < \lambda\}$, where the final choice of λ relies on a data-driven method so that it will be a random variable. To illustrate the idea briefly, we temporarily let $\lambda > 0$ be an non-random number. We now apply FDR control procedures to these two families of hypotheses. Let $\mathcal{B}_1 = \{i : |S_i| \geq \lambda\}$ and $\mathcal{B}_2 = \mathcal{B}_1^c$. For $i \in \mathcal{B}_1$, we reject H_{i0} if $|T_i| \geq t_1$ for some $t_1 > 0$, and for $i \in \mathcal{B}_2$, reject H_{i0} if $|T_i| \geq t_2$ for some $t_2 > 0$. Define the false discovery proportions for the two families of hypotheses by

$$\begin{aligned} FDP_{1,\lambda}(t) &= \frac{\sum_{i \in \mathcal{H}_0} I\{|S_i| \geq \lambda, |T_i| \geq t\}}{\max(1, \sum_{i=1}^m I\{|S_i| \geq \lambda, |T_i| \geq t\})}, \\ FDP_{2,\lambda}(t) &= \frac{\sum_{i \in \mathcal{H}_0} I\{|S_i| < \lambda, |T_i| \geq t\}}{\max(1, \sum_{i=1}^m I\{|S_i| < \lambda, |T_i| \geq t\})}, \end{aligned}$$

where $I\{\cdot\}$ is an indicator function and $\mathcal{H}_0 = \{1 \leq i \leq m : \mu_{i,1} = \mu_{i,2}\}$. To control the FDR/FDP at level α for these two families, as the B-H method, the ideal choices for t_1 and t_2 are

$$\hat{t}_1^\circ = \inf \left\{ t \geq 0 : FDP_{1,\lambda}(t) \leq \alpha \right\} \quad \text{and} \quad \hat{t}_2^\circ = \inf \left\{ t \geq 0 : FDP_{2,\lambda}(t) \leq \alpha \right\},$$

respectively. It is clearly $\sum_{i \in \mathcal{H}_0} I\{|S_i| \geq \lambda, |T_i| \geq t\}$ and $\sum_{i \in \mathcal{H}_0} I\{|S_i| < \lambda, |T_i| \geq t\}$ are unknown. Since S_i is asymptotically uncorrelated with T_i , we will show that under certain conditions, the above two terms can be approximated by $\hat{m}_{1,\lambda}^o(2 - 2\Psi(t))$ and $\hat{m}_{2,\lambda}^o(2 - 2\Psi(t))$, where

$$\hat{m}_{1,\lambda}^o = \sum_{i \in \mathcal{H}_0} I\{|S_i| \geq \lambda\} \quad \text{and} \quad \hat{m}_{2,\lambda}^o = m_0 - \hat{m}_{1,\lambda}^o$$

with $m_0 = |\mathcal{H}_0|$. It is straightforward to bound them by $\hat{m}_{1,\lambda}(2 - 2\Psi(t))$ and $\hat{m}_{2,\lambda}(2 - 2\Psi(t))$, where

$$\hat{m}_{1,\lambda} = \sum_{i=1}^m I\{|S_i| \geq \lambda\}, \quad \hat{m}_{2,\lambda} = m - \hat{m}_{1,\lambda}.$$

Using $\hat{m}_{1,\lambda}$ and $\hat{m}_{2,\lambda}$, we introduce the FDR control procedure as follow.

FDR control with US testing. Let

$$\begin{aligned} \hat{t}_{1,\lambda} &= \inf \left\{ t \geq 0 : \frac{\hat{m}_{1,\lambda}(2 - 2\Psi(t))}{\max(1, \sum_{i=1}^m I\{|S_i| \geq \lambda, |T_i| \geq t\})} \leq \alpha \right\}, \\ \hat{t}_{2,\lambda} &= \inf \left\{ t \geq 0 : \frac{\hat{m}_{2,\lambda}(2 - 2\Psi(t))}{\max(1, \sum_{i=1}^m I\{|S_i| < \lambda, |T_i| \geq t\})} \leq \alpha \right\}. \end{aligned}$$

We reject those H_{i0} if $i \in \mathcal{R}_\lambda$, where

$$\mathcal{R}_\lambda = \left\{ 1 \leq i \leq m : I\{|S_i| \geq \lambda, |T_i| \geq \hat{t}_{1,\lambda}\} = 1 \text{ or } I\{|S_i| < \lambda, |T_i| \geq \hat{t}_{2,\lambda}\} = 1 \right\}.$$

Note that if $\mu_{i,1} = \mu_{i,2} = 0$, then $P(|S_i| \geq 4\sqrt{\log m}) = O(m^{-8})$. So we only consider $0 \leq \lambda \leq 4\sqrt{\log m}$. Let N be a fixed positive integer and $\lambda_i = (i/N)\sqrt{\log m}$. The final screen level is selected by maximizing the number of rejections, i.e.,

$$\hat{\lambda} = (\hat{i}/N)\sqrt{\log m}, \quad \text{where} \quad \hat{i} = \arg \max_{0 \leq i \leq 4N} |\mathcal{R}_{\lambda_i}|.$$

If there are several i attain the maximum value, we choose \hat{i} to be the largest one among them. Based on $\hat{\lambda}$, we can obtain $\mathcal{R}_{\hat{\lambda}}$ and the final FDR control procedure is as follow.

FDR control with US testing. For a target FDR $0 < \alpha < 1$, reject H_{i0} if and only if $i \in \mathcal{R}_{\hat{\lambda}}$.

The simulation shows that the performance of the procedure is quite insensitive to the choice of N when $N \geq 10$.

3 Theoretical results

3.1 FDR and FDP control

In this section, we state some theoretical results for the US testing procedure. Let $\mathcal{H}_1 = \{1 \leq i \leq m : \mu_{i,1} \neq \mu_{i,2}\}$. The following conditions are needed to establish the main results.

(C1). $|\mathcal{H}_1| = o(m)$ as $m \rightarrow \infty$.

(C2). Assume that $\mathbb{E} \exp(t_0 |X_{i,j} - \mu_{i,j}| / \sigma_{i,j}) \leq K_1$ for some $K_1 > 0$, $t_0 > 0$, all $1 \leq i \leq m$ and $j = 1, 2$. Suppose that $c_1 \leq n_1/n_2 \leq c_2$ and $c_1 \leq \sigma_{i,1}^2/\sigma_{i,2}^2 \leq c_2$ for some $c_1, c_2 > 0$ and all $1 \leq i \leq m$. The sample sizes satisfy $\min(n_1, n_2) \geq c(\log m)^\zeta$ for some $\zeta > 5$ and $c > 0$.

In (C1), we assume that the mean difference $\boldsymbol{\mu}_1 - \boldsymbol{\mu}_2$ is sparse. The sparsity commonly arise from many applications such as the selection of differential expression genes. (C2) is a moment condition for populations which is regular in high-dimensional setting. Let \mathcal{M}_i be a subset of \mathcal{H}_0 such that $\{(X_{j,1}, X_{j,2}), j \in \mathcal{M}_i\}$ is independent with $(X_{i,1}, X_{i,2})$.

(C3). For every $i \in \mathcal{H}_0$, $|\mathcal{M}_i| \geq m_0 - K$ for some $K > 0$.

In (C3), for any $X_{i,1}$ and $X_{i,2}$, we allow K variables which can be strongly correlated with them. Define

$$\mathcal{R}_{0,\lambda} = \left\{ i \in \mathcal{H}_0 : I\{|S_i| \geq \lambda, |T_i| \geq \hat{t}_{1,\lambda}\} = 1 \text{ or } I\{|S_i| < \lambda, |T_i| \geq \hat{t}_{2,\lambda}\} = 1 \right\}.$$

The FDP and FDR for the US procedure are

$$FDP = \frac{|\mathcal{R}_{0,\hat{\lambda}}|}{\max(1, |\mathcal{R}_{\hat{\lambda}}|)} \quad \text{and} \quad FDR = \mathbb{E}[FDP].$$

Theorem 3.1 *Assume that (C2) and (C3) hold. Suppose that*

$$|\mathcal{R}_{\hat{\lambda}}| \rightarrow \infty \quad \text{in probability} \tag{1}$$

as $m \rightarrow \infty$. We have for any $\varepsilon > 0$,

$$P(FDP \leq \alpha + \varepsilon) \rightarrow 1 \tag{2}$$

as $m \rightarrow \infty$. Consequently, $\limsup_{m \rightarrow \infty} FDR \leq \alpha$.

Theorem 3.1 shows that the US procedure controls the FDR and FDP at level α asymptotically. We now discuss condition (1). Actually, if the p-values p_j , $j \in \mathcal{H}_{i0}$, are i.i.d. $U(0, 1)$ random variables, then Ferreira and Zwinderman (2006) prove that

$$\hat{R}_{BH} \rightarrow \infty \quad \text{in probability} \quad (3)$$

if and only if $FDP_{BH} \rightarrow \frac{m_0}{m}\alpha$ in probability, where FDP_{BH} is the false discovery proportion of the B-H method and \hat{R}_{BH} is the number of rejections. So (3) is a sufficient and necessary condition for the FDP control of the B-H method. By the definition of the US procedure, $|\mathcal{R}_0| = \hat{R}_{BH}$, and hence (3) implies (1). Therefore, we conjecture that (1) is also a nearly necessary condition for the FDP control (2). A sufficient condition for (1) and (3) is

$$Card\left\{1 \leq i \leq m : \frac{|\mu_{i,1} - \mu_{i,2}|}{\sqrt{\sigma_{i,1}^2/n_1 + \sigma_{i,2}^2/n_2}} \geq \theta\sqrt{\log m}\right\} \rightarrow \infty \quad \text{for some } \theta > \sqrt{2}, \quad (4)$$

which is quite mild.

3.2 Power comparison

In this section, we compare the US procedure to the B-H method. Define the power of the B-H method by

$$\text{power}_{BH} = \frac{\sum_{i \in \mathcal{H}_1} \mathbf{I}\{p_i \leq p_{(\hat{k})}\}}{m_1},$$

where $p_i = 2 - 2\Psi(|T_i|)$ and $m_1 = |\mathcal{H}_1|$. The power of the US procedure is defined by

$$\text{power}_{US} = \frac{|\mathcal{R}_{\hat{\lambda}}| - |\mathcal{R}_{0,\hat{\lambda}}|}{m_1}. \quad (5)$$

We first show that the US procedure can be at least as powerful as the B-H method asymptotically without requiring any sparsity on $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$.

Theorem 3.2 *Assume $m_1 \rightarrow \infty$ and (C1)-(C3) hold. Then we have*

$$\text{power}_{US} \geq \text{power}_{BH} + o_P(1)$$

for some $o_P(1)$ as $m \rightarrow \infty$.

The condition $m_1 \rightarrow \infty$ is a necessary condition for the FDP control of the B-H method; see Proposition 2.1 in Liu and Shao (2014). When m_1 is fixed as $m \rightarrow \infty$, the true FDPs of the B-H method and the US procedure will suffer from drastic fluctuations, and hence in this case we do not consider the power comparison under the FDP control. On the other hand, theoretical derivations for the power comparison under FDR control are typically more complicated when m_1 is fixed. We leave this as a future work.

We next investigate the power of the B-H method. Assume that

$$\frac{|\mu_{i,1} - \mu_{i,2}|}{\sqrt{\sigma_{i,1}^2/n_1 + \sigma_{i,2}^2/n_2}} = \theta \sqrt{\log m}, \quad i \in \mathcal{H}_1 \quad (6)$$

for some $\theta > 0$. The number of signals is assumed to be

$$|\mathcal{H}_1| = p^\beta \quad \text{for some } 0 < \beta < 1. \quad (7)$$

We have the following theorem for power_{BH} .

Theorem 3.3 *Suppose that (C2) and (C3) hold. If $0 < \theta < \sqrt{2(1-\beta)}$, then we have $\text{power}_{BH} \rightarrow 0$ in probability as $m \rightarrow \infty$. If $\theta > \sqrt{2(1-\beta)}$, then $\text{power}_{BH} \rightarrow 1$ in probability as $m \rightarrow \infty$.*

Theorem 3.3 reveals an interesting critical phenomenon for the B-H method. It indicates that when the size of signals satisfies $0 < \theta < \sqrt{2(1-\beta)}$, then the B-H method is unable to detect most of signals. On the other hand, if $\theta > \sqrt{2(1-\beta)}$, then the power of the B-H method converges to one. In this case, by Theorem 3.2, power_{US} will also converges to one in probability.

We shall show that, when $0 < \theta < \sqrt{2(1-\beta)}$, power_{US} can converge to one for a wide class of $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$. To this end, assume that $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$ satisfy

$$\text{Card}\left\{i \in \mathcal{H}_0 : \sqrt{\frac{n_1}{\sigma_{i,1}^2(1 + \frac{n_2\sigma_{i,1}^2}{n_1\sigma_{i,2}^2})}} \left| \mu_{i,1} + \frac{n_2\sigma_{i,1}^2}{n_1\sigma_{i,2}^2} \mu_{i,2} \right| \geq h\sqrt{\log m}\right\} = O(m^\gamma) \quad (8)$$

and

$$\text{Card}\left\{i \in \mathcal{H}_1 : \sqrt{\frac{n_1}{\sigma_{i,1}^2(1 + \frac{n_2\sigma_{i,1}^2}{n_1\sigma_{i,2}^2})}} \left| \mu_{i,1} + \frac{n_2\sigma_{i,1}^2}{n_1\sigma_{i,2}^2} \mu_{i,2} \right| \geq \kappa\sqrt{\log m}\right\} \geq \rho|\mathcal{H}_1| \quad (9)$$

for some $0 \leq \gamma \leq 1$, $0 < h \leq 2$, $0 < \rho \leq 1$ and $\kappa > h + \sqrt{2(1 - \beta)}$. (8) is an asymptotic sparsity condition on $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$. It is quite mild as m^γ elements can be arbitrarily large and the other elements can be of the order of $\sqrt{(\log m)/n}$. Condition (9) is needed to ensure that signals in \mathcal{H}_1 can be screened into the first family of hypotheses by S_i .

Theorem 3.4 *Suppose that (C2), (C3), (6) and (7) hold.*

- (i). *If $\theta > \sqrt{2(1 - \beta)}$, then $\text{power}_{US} \rightarrow 1$ in probability as $m \rightarrow \infty$.*
- (ii). *Assume that (8) and (9) hold. Let $\theta > \sqrt{\max(0, 2\gamma - 2\beta)}$ and $N \geq 10/\min(1 - \beta, \theta^2/4)$. We have $P(\text{power}_{US} \geq \rho - \varepsilon) \rightarrow 1$ for any $\varepsilon > 0$ as $m \rightarrow \infty$.*
- (iii). *We have $P(FDP \leq \alpha + \varepsilon) \rightarrow 1$ for any $\varepsilon > 0$ as $m \rightarrow \infty$.*

Theorem 3.4 indicates that, if $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$ satisfy (8) and (9), then power_{US} can be much larger than power_{BH} . In particular, the power of US procedure converges to one when $\rho = 1$ and $\theta > \sqrt{\max(0, 2\gamma - 2\beta)}$. In contrast, if $\sqrt{\max(0, 2\gamma - 2\beta)} < \theta < \sqrt{2(1 - \beta)}$, power_{BH} converges to zero.

Remark. Condition (8) is quite mild. For example, in ultra-high dimensional setting $\log m \geq c \max(n_1, n_2)$ for some $c > 0$, all of components of $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$ can be bounded away from zero. In this case, (8) essentially is not an asymptotic sparsity condition. In (C2), we require $\min(n_1, n_2) \geq c(\log m)^\zeta$ for some $\zeta > 5$. However, this condition is only used to ensure that the sample variances and null distribution of T_i are close to the population variances and $\Psi(t)$, respectively. In the ideal case that \mathbf{X}_1 and \mathbf{X}_2 are multivariate normal random vectors with known variances, we can use $T_{0i} = (\bar{X}_{i,1} - \bar{X}_{i,2})/\sqrt{\sigma_{i,1}^2/n_1 + \sigma_{i,2}^2/n_2}$ as a test statistic with $N(0, 1)$ null distribution and S_{0i} as a screening statistic. Then all theorems hold without (C2). In this case, (8) allows non-sparse $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$ in ultra-high dimensional setting. Although \mathbf{X}_1 and \mathbf{X}_2 may be non-Gaussian, we will show by numerical studies in Section 4 that the US procedure indeed outperforms the B-H method for non-sparse mean vectors when m is large.

4 Numerical results

In this section, we conduct numerical simulations and examine the performance of the US procedure. Let

$$\mathbf{X}_1 = \boldsymbol{\mu}_1 + \boldsymbol{\varepsilon}_1 - \mathbf{E}\boldsymbol{\varepsilon}_1 \quad \text{and} \quad \mathbf{X}_2 = \boldsymbol{\mu}_1 + \boldsymbol{\varepsilon}_2 - \mathbf{E}\boldsymbol{\varepsilon}_2,$$

where $\boldsymbol{\varepsilon}_1 = (\varepsilon_{1,1}, \dots, \varepsilon_{m,1})$ and $\boldsymbol{\varepsilon}_2 = (\varepsilon_{1,2}, \dots, \varepsilon_{m,2})$ are independent random vectors.

Model 1. Let $\mu_{i,1} = 3\sqrt{\frac{\log m}{n_1}}$ and $\mu_{i,2} = 2\sqrt{\frac{\log m}{n_2}}$ for $1 \leq i \leq m_1$; $\mu_{i,1} = \mu_{i,2} = 0$ for $m_1 + 1 \leq i \leq m$.

Model 2. Let $\mu_{i,1} = 2\sqrt{\frac{\log m}{n_1}}$ for $1 \leq i \leq m_1$; $\mu_{i,2} = \sqrt{\frac{\log m}{n_2}}$ for $1 \leq i \leq [m_1/2]$; $\mu_{i,2} = -0.5\sqrt{\frac{\log m}{n_2}}$ for $[m_1/2] + 1 \leq i \leq m_1$; $\mu_{i,1} = \mu_{i,2} = 0$ for $m_1 + 1 \leq i \leq m$.

Model 3. Let $\mu_{i,1} = 3\sqrt{\frac{\log m}{n_1}}$ and $\mu_{i,2} = 2\sqrt{\frac{\log m}{n_2}}$ for $1 \leq i \leq m_1$; $\mu_{i,1} = \mu_{i,2} = (i/m)\sqrt{(\log m)/n_1}$ for $m_1 + 1 \leq i \leq m$.

Model 4. Let $\mu_{i,1} = 3\sqrt{\frac{\log m}{n_1}}$ and $\mu_{i,2} = 2\sqrt{\frac{\log m}{n_2}}$ for $1 \leq i \leq m_1$; $\mu_{i,1} = \mu_{i,2} = 1$ for $m_1 + 1 \leq i \leq m_1 + [\sqrt{m}]$; $\mu_{i,1} = \mu_{i,2} = 0.2$ for $m_1 + [\sqrt{m}] + 1 \leq i \leq m$.

In Models 1 and 2, $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$ are exactly sparse, and they are asymptotically sparse in Model 3. In Model 4, $\boldsymbol{\mu}_1$ and $\boldsymbol{\mu}_2$ are non-sparse vectors. We take $n_1 = n_2 = 100$, $p = 2000$ and $m_1 = [\sqrt{m}]$. We consider the US procedure for *equal variances case* and *unequal variances case*. In the first case, we let $\varepsilon_{i,1}$ and $\varepsilon_{i,2}$, $1 \leq i \leq m$, be i.i.d. $N(0, 1)$ variables. In the second case, $\varepsilon_{i,1} \sim N(0, 0.5)$ and $\varepsilon_{i,2} \sim N(0, 1)$. We also carry out simulation studies for t -distributed errors and simulation results are stated in the supplementary material Liu (2014).

The simulation is replicated 500 times and N in $\hat{\lambda}$ is taken to be 10. Extensive simulations indicate that the performance of the US procedure is quite insensitive to the choice of N when $N \geq 10$. We calculate the empirical powers of the US procedure and the B-H method by

$$\text{power}_{US} = \frac{1}{500} \sum_{i=1}^{500} \text{power}_{US,i} \quad \text{and} \quad \text{power}_{BH} = \frac{1}{500} \sum_{i=1}^{500} \text{power}_{BH,i},$$

where $\text{power}_{US,i}$ and $\text{power}_{BH,i}$ are the powers of the US procedure and the B-H method in the i -th replication, respectively. Also, the empirical FDRs are obtained by the average of all FDPs in 500 replications:

$$\text{eFDR}_{US} = \frac{1}{500} \sum_{i=1}^{500} \text{FDP}_{US,i} \quad \text{and} \quad \text{eFDR}_{BH} = \frac{1}{500} \sum_{i=1}^{500} \text{FDP}_{BH,i},$$

The target FDR is taken to be $\alpha = i/20$, $1 \leq i \leq 20$ so that we can compare the US procedure and the B-H method along a series of α . The empirical powers power_{US} and power_{BH} are plotted in Figures 1 and 2 for all $\alpha = i/20$, $1 \leq i \leq 20$. From Figures 1

and 2, we can see that the US procedure has much more statistical power than the B-H method on all four models. For example, in Model 1, power_{BH} is below 0.1 for $\alpha \leq 0.3$, while power_{US} grows from 0.3 to 0.7 as α grows from 0.05 to 0.3. Similar phenomenon can be observed for other models. In particular, for the non-sparse Model 4, the US procedure is still significantly more powerful than the B-H method.

To examine the performance of FDR control, we consider the ratio between the empirical FDR and the target FDR α . The values eFDR/α are plotted in Figures 3 and 4. We can see that the ratios for Models 1-4 are always close to or smaller than 1. Hence, the US procedure can control the FDR effectively while having more power than the B-H method. Note that in many cases, the FDRs of the US procedure are smaller than α . The possible reason is that $\hat{m}_{1,\lambda}$ overestimates $\hat{m}_{1,\lambda}^o$ as \mathcal{B}_1 usually contains more true alternatives than true nulls. So the FDR in the first family of hypotheses will be smaller than α . Overall, the US procedure is much more powerful than the B-H method, and interestingly, it has smaller FDRs when $\alpha \leq 0.5$.

We next examine the performance of other seemingly natural screening methods including the square type screening statistics and maximum type screening statistics. Let $T_{i,1}$ and $T_{i,2}$ be one-sample *Student's* statistics $T_{i,1} = \sqrt{n_1}\bar{X}_{i,1}/\hat{\sigma}_{i,1}$ and $T_{i,2} = \sqrt{n_2}\bar{X}_{i,2}/\hat{\sigma}_{i,2}$. The square type screening and maximum type screening use $SS_i = \sqrt{T_{i,1}^2 + T_{i,2}^2}$ and $MS_i = \max(|T_{i,1}|, |T_{i,2}|)$ as screening statistics, respectively. Now we replace S_i in the US procedure by SS_i and MS_i and replicate the above numerical studies for Model 4. The screen level λ is chosen to be $\hat{\lambda}$ or $\sqrt{2\log m}$. The ratios eFDR/α are plotted in Figure 5. We can see that neither the square type screening nor the maximum type screening controls the FDR. The reason is that SS_i and MS_i are correlated with T_i so that p-values are no longer $U(0, 1)$ after screening.

Finally, we show that *testing after screening* with sample splitting may loss much statistical power. To see this, we consider the following model.

Model 5. Let $\mu_{i,1} = 1.5\sqrt{\frac{\log m}{n_1}}$ and $\mu_{i,2} = -0.5\sqrt{\frac{\log m}{n_1}}$ for $1 \leq i \leq \lfloor \sqrt{m} \rfloor$; $\mu_{i,1} = \mu_{i,2} = 0$ for $\lfloor \sqrt{m} \rfloor + 1 \leq i \leq m$.

In the screening stage, we use 50 samples to construct screening statistics SS_i and MS_i . The two-sample *Student's* statistics T_i are constructed from the remaining 50 samples. The thresholding level in screening stage is chosen by the same way as $\hat{\lambda}$. We plot power curves in Figure 6 for SS_i screening and MS_i screening. It can be observed that the

sample splitting method results in a significant power loss, comparing to the B-H method and the US procedure.

5 Discussion

In this article, we consider the FDR/FDP control for two-sample multiple t tests. The proposed US procedure is shown to be more powerful than the classical B-H method. There are several possible extensions.

In the setting of dense signals, it is well known that an accurate estimator for the number of true null hypotheses can help improve the power of the B-H method; see Storey, et al. (2004). The latter paper develops an estimator \hat{m}_0 for m_0 and then incorporates it into the B-H method. Similarly, we can develop some accurate estimates for $\hat{m}_{1,\lambda}^o$ and $\hat{m}_{2,\lambda}^o$ to replace $\hat{m}_{1,\lambda}$ and $\hat{m}_{2,\lambda}$. The power of the US procedure is expected to be improved in this way and theoretical study is left for future work.

Controlling the FDR under dependence is an important and challenging topic. Many procedures for FDR control under various dependence frameworks have been developed. Leek and Storey (2008) consider a general framework for multiple tests in the presence of arbitrarily strong dependence. Friguet, et al. (2009) consider the FDR control under the factor model assumption. Fan, et al. (2012) estimate the false discovery proportion under arbitrary covariance dependence. It would be interesting to study the US procedure under these dependence settings.

The uncorrelated screening technique can be extended to other related two-sample testing problems. For example, consider the two sample correlation testing problem $H_{0ij} : \rho_{ij1} = \rho_{ij2}$, $1 \leq i < j \leq m$, where $\mathbf{R}_1 = (\rho_{ij1})_{1 \leq i, j \leq m}$ and $\mathbf{R}_2 = (\rho_{ij2})_{1 \leq i, j \leq m}$ are two correlation matrices. The correlation matrix is often assumed to be (asymptotically) sparse; see Bickel and Levina (2008). The uncorrelated screening technique can be applied in this problem. Similarly, it can be applied in two sample partial correlation testing problem $H_{0ij} : \rho'_{ij1} = \rho'_{ij2}$, $1 \leq i < j \leq m$, where ρ'_{ij1} and ρ'_{ij2} denote the partial correlation coefficients which are closely related to Gaussian graphical models (GGM). In GGM estimation, it is common to assume the sparsity on the partial correlation coefficients; see Liu (2013).

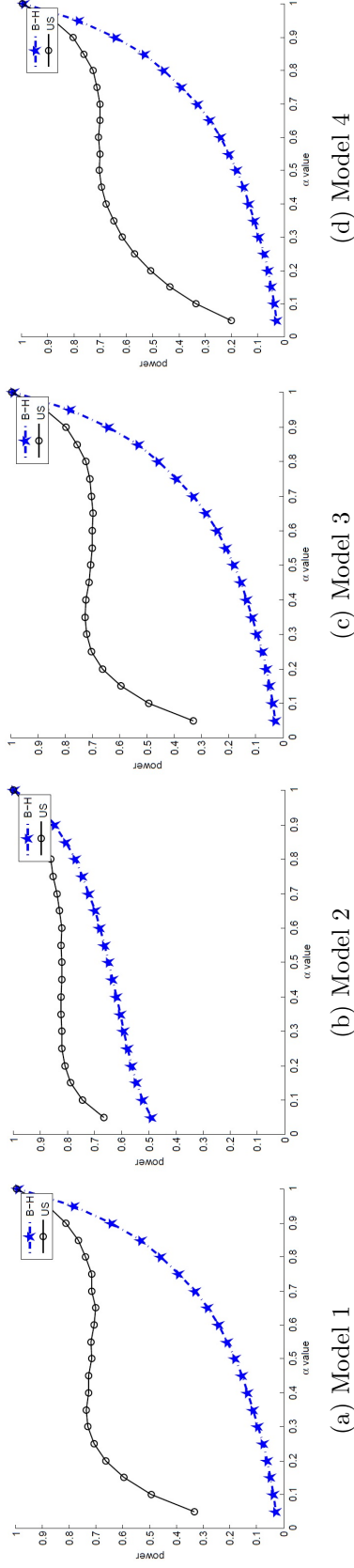


Figure 1: Equal variances. The x-axis denotes the α value and the y-axis denotes the power.

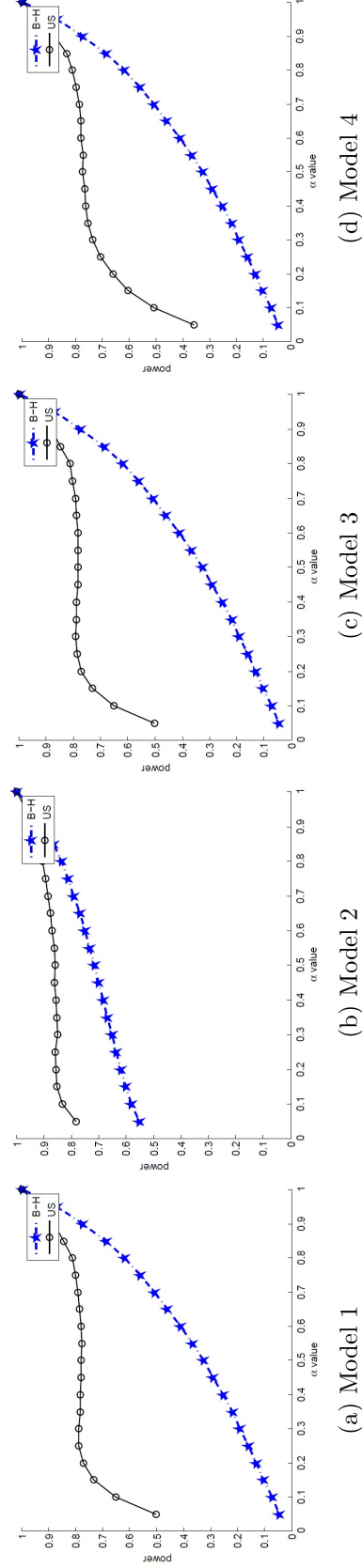


Figure 2: Unequal variances. The x-axis denotes the α value and the y-axis denotes the power.

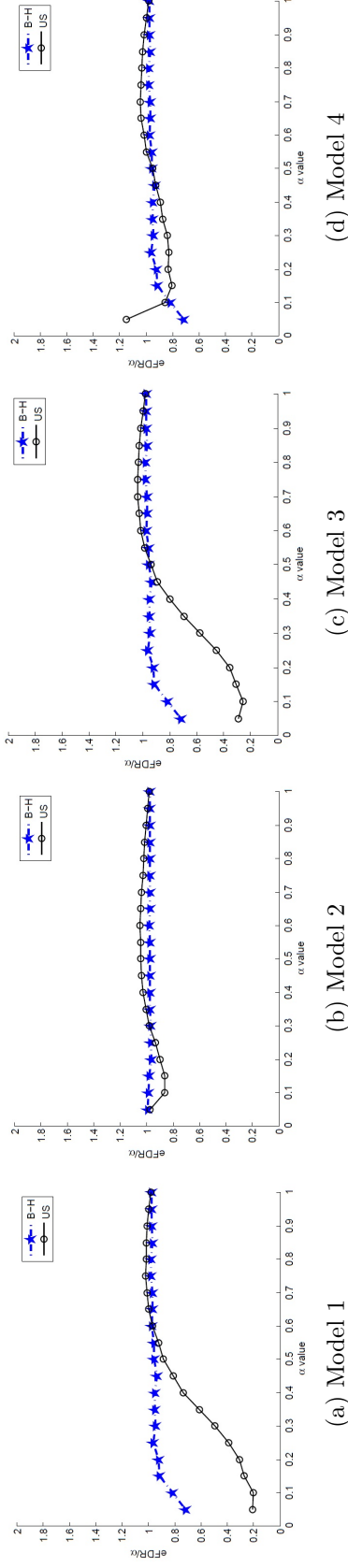


Figure 3: Equal variances. The x-axis denotes the α value and the y-axis denotes $eFDR/\alpha$.

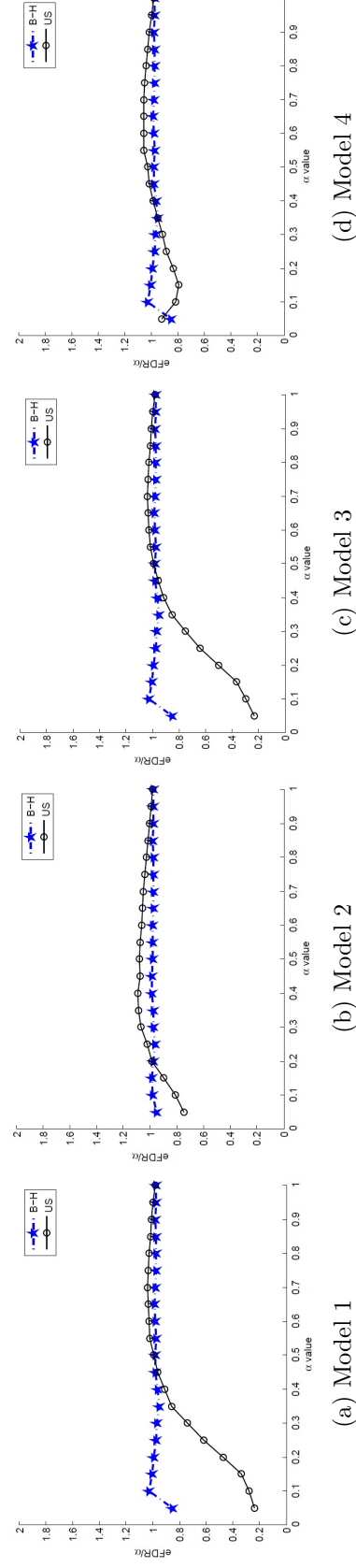


Figure 4: Unequal variances. The x-axis denotes the α value and the y-axis denotes $eFDR/\alpha$.

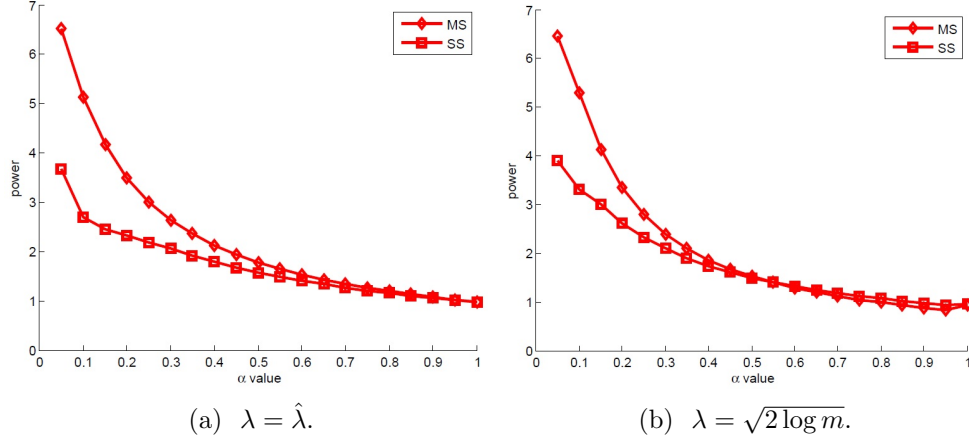


Figure 5: Model 4 and equal variances. The x-axis denotes the α value and the y-axis denotes eFDR/α by screening with SS_i and MS_i .

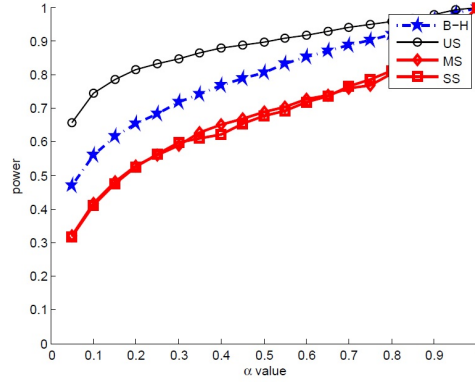


Figure 6: Model 5 and equal variances. The x-axis denotes the α value and the y-axis denotes the powers of the US procedure, the B-H procedure and the sample splitting method with MS_i and SS_i screening.

6 Proof of main results

We only prove the main results for Case II, variances $\sigma_{i,1}^2$ and $\sigma_{i,2}^2$ are not necessary equal because the proof for Case I is quite similar.

6.1 Proof of Theorem 3.1

Let $c_m \rightarrow \infty$ such that $\mathbb{P}(|\mathcal{R}_{\hat{\lambda}}| \geq c_m) \rightarrow 1$ as $m \rightarrow \infty$. Define

$$m_{1,\lambda}^o = \sum_{i \in \mathcal{H}_0} \mathbb{P}(|N(0,1) + h_i| \geq \lambda) \quad \text{and} \quad m_{2,\lambda}^o = \sum_{i \in \mathcal{H}_0} \mathbb{P}(|N(0,1) + h_i| < \lambda),$$

where

$$h_i = \sqrt{\frac{n_1}{\sigma_{i,1}^2(1 + \frac{n_2\sigma_{i,1}^2}{n_1\sigma_{i,2}^2})}} \left(\mu_{i,1} + \frac{n_2\sigma_{i,1}^2}{n_1\sigma_{i,2}^2} \mu_{i,2} \right).$$

We first prove that for any $b_m \rightarrow \infty$, $\varepsilon > 0$ and $0 \leq \lambda \leq 4\sqrt{\log m}$,

$$\mathbb{P}\left(\sup_{0 \leq t \leq G^{-1}(b_m/m_{1,\lambda}^o)} \left| \frac{\sum_{i \in \mathcal{H}_0} I\{|S_i| \geq \lambda, |T_i| \geq t\}}{m_{1,\lambda}^o G(t)} - 1 \right| \geq \varepsilon\right) \rightarrow 0 \quad (10)$$

as $m \rightarrow \infty$, where $G(t) = 2 - 2\Psi(t)$ and $\sup_{0 \leq t \leq G^{-1}(b_m/m_{1,\lambda}^o)}(\cdot) = 0$ if $b_m > m_{1,\lambda}^o$. Note that we only need to consider the case $m_{1,\lambda}^o \geq b_m$. By (19), (22), (24) and the proof of Lemma 6.3 in Liu (2013), it suffices to prove for any $\varepsilon > 0$,

$$\int_0^{G^{-1}(b_m/m_{1,\lambda}^o)} \mathbb{P}\left(\left| \frac{\sum_{i \in \mathcal{H}_0} f_i(\lambda, t)}{m_{1,\lambda}^o G(t)} \right| \geq \varepsilon\right) I\{m_{1,\lambda}^o \geq b_m\} dt = o(v_m) \quad (11)$$

for some $v_m = o(1/\sqrt{\log m_{1,\lambda}^o})$ and

$$\sup_{0 \leq t \leq G^{-1}(b_m/m_{1,\lambda}^o)} \mathbb{P}\left(\left| \frac{\sum_{i \in \mathcal{H}_0} f_i(\lambda, t)}{m_{1,\lambda}^o G(t)} - 1 \right| \geq \varepsilon\right) I\{m_{1,\lambda}^o \geq b_m\} = o(1) \quad (12)$$

as $m \rightarrow \infty$, where $\log(x) = \ln(\max(x, e))$ and

$$f_i(\lambda, t) = I\{|S_i| \geq \lambda, |T_i| \geq t\} - \mathbb{P}(|S_i| \geq \lambda, |T_i| \geq t).$$

By Lemma 6.2 and (C3), we have for any $M > 0$,

$$\mathbb{E}(f_i(\lambda, t))^2 \leq C\{m_{1,\lambda}^o G(t) + m^{-M}\}$$

uniformly in $0 \leq t \leq 4\sqrt{\log m}$, $0 \leq \lambda \leq 4\sqrt{\log m}$ and $i \in \mathcal{H}_0$. This proves (12). Note that

$$\int_0^{G^{-1}(b_m/m_{1,\lambda}^o)} \frac{1}{m_{1,\lambda}^o G(t)} dt \leq \frac{C}{b_m \sqrt{\log(m_{1,\lambda}^o/b_m)}}.$$

Thus, we have (11). By Lemma 6.3, we have

$$\mathbb{P}\left(\sup_{0 \leq t \leq G^{-1}(b_m/m_{1,\lambda}^o)} \left| \frac{\sum_{i \in \mathcal{H}_0} I\{|S_i| \geq \lambda, |T_i| \geq t\}}{\hat{m}_{1,\lambda}^o G(t)} - 1 \right| \geq \varepsilon\right) \rightarrow 0 \quad (13)$$

as $m \rightarrow \infty$. Similarly, we can show that for any $b_m \rightarrow \infty$ and all $0 \leq j \leq 4N$,

$$\mathbb{P}\left(\sup_{0 \leq t \leq G^{-1}(b_m/m_{2,\lambda_j}^o)} \left| \frac{\sum_{i \in \mathcal{H}_0} I\{|S_i| < \lambda_j, |T_i| \geq t\}}{\hat{m}_{2,\lambda_j}^o G(t)} - 1 \right| \geq \varepsilon\right) \rightarrow 0 \quad (14)$$

as $m \rightarrow \infty$. By the definition of $\hat{t}_{1,\lambda}$, we have

$$\hat{m}_{1,\lambda} G(\hat{t}_{1,\lambda}) = \alpha \max\left(1, \sum_{i=1}^m I\{|S_i| \geq \lambda, |T_i| \geq \hat{t}_{1,\lambda}\}\right).$$

Hence, by (13) and Lemma 6.3, for any $\varepsilon > 0$, $b_m \rightarrow \infty$,

$$\mathbb{P}\left(FDP_{1,\lambda}(\hat{t}_{1,\lambda}) \geq (1 + \varepsilon)\alpha, m_{1,\lambda}^o G(\hat{t}_{1,\lambda}) \geq b_m\right) \rightarrow 0 \quad (15)$$

as $m \rightarrow \infty$. Similarly, for any $0 \leq j \leq 4N$, $\varepsilon > 0$ and $b_m \rightarrow \infty$,

$$\mathbb{P}\left(FDP_{2,\lambda_j}(\hat{t}_{2,\lambda_j}) \geq (1 + \varepsilon)\alpha, m_{2,\lambda_j}^o G(\hat{t}_{2,\lambda_j}) \geq b_m\right) \rightarrow 0 \quad (16)$$

as $m \rightarrow \infty$. Define

$$FDP_\lambda = \frac{|\mathcal{R}_{0,\lambda}|}{\max(1, |\mathcal{R}_\lambda|)}.$$

Then

$$\mathbb{P}\left(FDP_\lambda \geq (1 + \varepsilon)\alpha, m_{i,\lambda}^o G(\hat{t}_{i,\lambda}) \geq b_m, i = 1, 2\right) \rightarrow 0. \quad (17)$$

It follows that

$$\begin{aligned} & \mathbb{P}\left(FDP_{\hat{\lambda}} \geq (1 + \varepsilon)\alpha, m_{i,\hat{\lambda}}^o G(\hat{t}_{i,\hat{\lambda}}) \geq b_m, i = 1, 2\right) \\ & \leq \sum_{j=0}^{4N} \mathbb{P}\left(FDP_{\lambda_j} \geq (1 + \varepsilon)\alpha, m_{i,\lambda_j}^o G(\hat{t}_{i,\lambda_j}) \geq b_m, i = 1, 2\right) \end{aligned}$$

$$\rightarrow 0. \quad (18)$$

Take $b_m^2 = o(c_m \wedge m)$. For $0 \leq \lambda \leq 4\sqrt{\log m}$, by Lemma 6.2 and Markov's inequality,

$$\begin{aligned} & \mathbb{P}\left(\sum_{i \in \mathcal{H}_0} I\{|S_i| \geq \lambda, |T_i| \geq \hat{t}_{1,\lambda}\} \geq b_m^2, m_{1,\lambda}^o G(\hat{t}_{1,\lambda}) < b_m\right) \\ & \leq \mathbb{P}\left(\sum_{i \in \mathcal{H}_0} I\{|S_i| \geq \lambda, |T_i| \geq G^{-1}(\min(1, b_m/m_{1,\lambda}^o))\} \geq b_m^2\right) \\ & \leq C/b_m \\ & \rightarrow 0. \end{aligned}$$

Hence, we have

$$\mathbb{P}\left(\sum_{i \in \mathcal{H}_0} I\{|S_i| \geq \hat{\lambda}, |T_i| \geq \hat{t}_{1,\hat{\lambda}}\} \geq b_m^2, m_{1,\hat{\lambda}}^o G(\hat{t}_{1,\hat{\lambda}}) < b_m\right) \rightarrow 0$$

as $m \rightarrow \infty$. Similarly,

$$\mathbb{P}\left(\sum_{i \in \mathcal{H}_0} I\{|S_i| < \hat{\lambda}, |T_i| \geq \hat{t}_{2,\hat{\lambda}}\} \geq b_m^2, m_{2,\hat{\lambda}}^o G(\hat{t}_{2,\hat{\lambda}}) < b_m\right) \rightarrow 0.$$

By $\mathbb{P}(|\mathcal{R}_{\hat{\lambda}}| \geq c_m) \rightarrow 1$, (15) and (16), it follows that

$$\mathbb{P}\left(FDP_{\hat{\lambda}} \geq (1 + \varepsilon)\alpha, m_{i,\hat{\lambda}}^o G(\hat{t}_{i,\hat{\lambda}}) < b_m\right) \rightarrow 0$$

for $i = 1, 2$ and any $\varepsilon > 0$. This, together with (18), proves that $\mathbb{P}(FDP_{\hat{\lambda}} \leq (1 + \varepsilon)\alpha) \rightarrow 1$ as $m \rightarrow \infty$. ■

The proofs of Lemmas 6.1-6.3 are given in the supplementary material Liu (2014).

Lemma 6.1 *We have for any $M > 0$,*

$$P(|S_i| \geq \lambda) = (1 + o(1))P(|N(0, 1) + h_i| \geq \lambda) + O(m^{-M}) \quad (19)$$

and

$$P(|T_i| \geq \lambda) = (1 + o(1))G(t) + O(m^{-M}), \quad (20)$$

uniformly in $0 \leq \lambda \leq 4\sqrt{\log m}$ and $i \in \mathcal{H}_0$. For $0 \leq j \leq 4N$,

$$P(|S_i| < \lambda_j) = (1 + o(1))P(|N(0, 1) + h_i| < \lambda_j) + O(m^{-M}) \quad (21)$$

uniformly in $i \in \mathcal{H}_0$.

Lemma 6.2 *We have for any $M > 0$,*

$$P(|S_i| \geq \lambda, |T_i| \geq t) = (1 + o(1))P(|N(0, 1) + h_i| \geq \lambda)G(t) + O(m^{-M}) \quad (22)$$

uniformly in $0 \leq \lambda \leq 4\sqrt{\log m}$, $0 \leq t \leq 4\sqrt{\log m}$ and $i \in \mathcal{H}_0$. For all $0 \leq j \leq 4N$,

$$P(|S_i| < \lambda_j, |T_i| \geq t) = (1 + o(1))P(|N(0, 1) + h_i| < \lambda_j)G(t) + O(m^{-M}) \quad (23)$$

uniformly in $0 \leq t \leq 4\sqrt{\log m}$ and $i \in \mathcal{H}_0$.

Lemma 6.3 *Let $b_m \rightarrow \infty$ be a sequence of positive numbers. (i). Assume that λ satisfies $0 \leq \lambda \leq 4\sqrt{\log m}$. We have*

$$P\left(\left|\frac{\hat{m}_{1,\lambda}^o}{m_{1,\lambda}^o} - 1\right| \geq \varepsilon\right)I\{m_{1,\lambda}^o \geq b_m\} \rightarrow 0 \quad \text{as } m \rightarrow \infty. \quad (24)$$

(ii). For $0 \leq j \leq 4N$,

$$P\left(\left|\frac{\hat{m}_{2,\lambda_j}^o}{m_{2,\lambda_j}^o} - 1\right| \geq \varepsilon\right)I\{m_{2,\lambda_j}^o \geq b_m\} \rightarrow 0 \quad \text{as } m \rightarrow \infty. \quad (25)$$

6.2 Proof of Theorem 3.2

By (10) with $\lambda = 0$, we have for any $b_m \rightarrow \infty$ and $\varepsilon > 0$,

$$P\left(\sup_{0 \leq t \leq G^{-1}(b_m/m_0)} \left|\frac{\sum_{i \in \mathcal{H}_0} I\{|T_i| \geq t\}}{m_0 G(t)} - 1\right| \geq \varepsilon\right) \rightarrow 0. \quad (26)$$

The B-H method is equivalent to reject H_{i0} if and only if $p_i \leq \hat{t}_{BH}$, where

$$\hat{t}_{BH} = \max \left\{ 0 \leq t \leq 1 : mt \leq \alpha \max \left(\sum_{i=1}^m I\{p_i \leq t\}, 1 \right) \right\}$$

and $p_i = G(|T_i|)$. By the definition of \hat{t}_{BH} , we have

$$m\hat{t}_{BH} = \alpha \max \left(\sum_{i=1}^m I\{p_i \leq \hat{t}_{BH}\}, 1 \right). \quad (27)$$

Let $\hat{R}_{BH} = \sum_{i=1}^m I\{p_i \leq \hat{t}_{BH}\}$ and $\hat{R}_{1,BH} = \sum_{i \in \mathcal{H}_1} I\{p_i \leq \hat{t}_{BH}\}$. By (26) and $m_1 = o(m)$, for any $\varepsilon > 0$ and $c_m \rightarrow \infty$ with $b_m^2 = o(c_m)$ and $c_m = o(m_1)$,

$$P\left(\left|\frac{FDP_{BH}}{\alpha} - 1\right| \geq \varepsilon, \hat{R}_{BH} \geq c_m\right) \rightarrow 0 \quad \text{as } m \rightarrow \infty.$$

Hence, for any $\varepsilon_1 > 0$, we have

$$\mathbf{P}\left(\hat{R}_{1,BH} \geq (1 - \alpha + \varepsilon_1)\hat{R}_{BH}, \hat{R}_{BH} \geq c_m\right) \rightarrow 0 \quad \text{as } m \rightarrow \infty. \quad (28)$$

Take $\varepsilon_1 > 0$ and $\varepsilon_2 > 0$ such that $(1 - \varepsilon)(1 - \alpha + \varepsilon_1) \leq (1 - \alpha - \alpha\varepsilon_2)$. Since $|\mathcal{R}_{\hat{\lambda}}| \geq \hat{R}_{BH}$, by the proof of Theorem 3.1, we have $\mathbf{P}(FDP \geq (1 + \varepsilon_2)\alpha, \hat{R}_{BH} \geq c_m) \rightarrow 0$. This implies that

$$\mathbf{P}(|\mathcal{R}_{\hat{\lambda}}| - |\mathcal{R}_{0,\hat{\lambda}}| \leq (1 - \alpha - \alpha\varepsilon_2)|\mathcal{R}_{\hat{\lambda}}|, \hat{R}_{BH} \geq c_m) \rightarrow 0. \quad (29)$$

It follows from (28) and (29) that

$$\mathbf{P}(\text{power}_{US} \leq (1 - \varepsilon)\text{power}_{BH}, \hat{R}_{BH} \geq c_m) \rightarrow 0$$

as $m \rightarrow \infty$. Note that $\mathbf{P}(\text{power}_{BH} \geq \varepsilon, \hat{R}_{BH} \leq c_m) \rightarrow 0$. So we have $\mathbf{P}(\text{power}_{US} \geq \text{power}_{BH} - \varepsilon) \rightarrow 1$ for any $\varepsilon > 0$. Theorem 3.2 is proved. ■

6.3 Proof of Theorem 3.3

For $\varepsilon > 0$, define

$$\mathbf{F}_1 = \left\{ \left| \frac{\sum_{i \in \mathcal{H}_0} I\{p_i \leq \hat{t}_{BH}\}}{m_0 \hat{t}_{BH}} - 1 \right| \leq \varepsilon \right\}$$

and $\mathbf{E}_1 = \{\hat{t}_{BH} \geq m^{-w}\}$ for some $0 < w < 1$, where $m_0 = |\mathcal{H}_0|$. By (10), we have for any $0 < w < 1$,

$$\sup_{m^{-w} \leq t \leq 1} \left| \frac{\sum_{i \in \mathcal{H}_0} I\{p_i \leq t\}}{m_0 t} - 1 \right| \rightarrow 0 \quad (30)$$

in probability as $m \rightarrow \infty$. Thus, $\mathbf{P}(\mathbf{E}_1 \cap \mathbf{F}_1^c) = o(1)$. On \mathbf{F}_1 , we have

$$m\hat{t}_{BH} = (\alpha + O(\varepsilon)) \left(\sum_{i \in \mathcal{H}_1} I\{p_i \leq \hat{t}_{BH}\} + m_0 \hat{t}_{BH} \right)$$

which implies that

$$\frac{\sum_{i \in \mathcal{H}_1} I\{p_i \leq \hat{t}_{BH}\}}{m\hat{t}_{BH}} = \alpha^{-1} - 1 + O(\varepsilon). \quad (31)$$

Hence, on \mathbf{F}_1 , we have $\hat{t}_{BH} \leq C_{\alpha,\varepsilon} m^{\beta-1}$. Let

$$T'_i = \frac{\bar{X}_{i,1} - \bar{X}_{i,2} - (\mu_{i,1} - \mu_{i,1})}{\sqrt{\hat{\sigma}_{i,1}^2/n_1 + \hat{\sigma}_{i,2}^2/n_2}}.$$

For $i \in \mathcal{H}_1$, we have

$$\begin{aligned}
I\{p_i \leq \hat{t}_{BH}\} &\leq I\{T'_i \geq G^{-1}(\hat{t}_{BH}) - \frac{\sqrt{\sigma_{i,1}^2/n_1 + \sigma_{i,2}^2/n_2}}{\sqrt{\hat{\sigma}_{i,1}^2/n_1 + \hat{\sigma}_{i,2}^2/n_2}} \theta \sqrt{\log m}\} \\
&\quad + I\{-T'_i \geq G^{-1}(\hat{t}_{BH}) - \frac{\sqrt{\sigma_{i,1}^2/n_1 + \sigma_{i,2}^2/n_2}}{\sqrt{\hat{\sigma}_{i,1}^2/n_1 + \hat{\sigma}_{i,2}^2/n_2}} \theta \sqrt{\log m}\} \\
&=: I_{i,1} + I_{i,2}.
\end{aligned}$$

Since $\theta < \sqrt{2(1-\beta)}$, by central limit theorem and (2) in the supplementary material Liu (2014),

$$g_{m,i} := \mathbb{P}\left(T'_i \geq G^{-1}(C_{\alpha,\varepsilon} m^{\beta-1}) - \frac{\sqrt{\sigma_{i,1}^2/n_1 + \sigma_{i,2}^2/n_2}}{\sqrt{\hat{\sigma}_{i,1}^2/n_1 + \hat{\sigma}_{i,2}^2/n_2}} \theta \sqrt{\log m}\right) \rightarrow 0$$

uniformly in $i \in \mathcal{H}_1$. By Markov's inequality,

$$\mathbb{P}\left(\frac{\sum_{i \in \mathcal{H}_1} I_{i,1}}{m_1} \geq \varepsilon, \mathbf{F}_1\right) \leq \varepsilon^{-1} \frac{\sum_{i \in \mathcal{H}_1} g_{m,i}}{m_1} = o(1). \quad (32)$$

Similarly,

$$\mathbb{P}\left(\frac{\sum_{i \in \mathcal{H}_1} I_{i,2}}{m_1} \geq \varepsilon, \mathbf{F}_1\right) = o(1).$$

On \mathbf{E}_1^c , we have $\hat{t}_{BH} < m^{-w} \leq m^{\beta-1}$, where we take $1-\beta < w < 1$. Hence, as in (32),

$$\mathbb{P}\left(\frac{\sum_{i \in \mathcal{H}_1} (I_{i,1} + I_{i,2})}{m_1} \geq \varepsilon, \mathbf{E}_1^c\right) = o(1).$$

This proves $power_{BH} \rightarrow 0$ in probability.

We next prove the theorem when $\theta > \sqrt{2(1-\beta)}$. So there exists some $\epsilon > 0$ such that $\theta > \sqrt{2(1-\beta+\epsilon)}$. Suppose that $\theta < \sqrt{2(1+\epsilon)}$. By (30), we have

$$\frac{\sum_{i \in \mathcal{H}_0} I\{p_i \leq m^{-\theta^2/2+\epsilon}\}}{m_0 m^{-\theta^2/2+\epsilon}} \rightarrow 1$$

in probability as $m \rightarrow \infty$. Also, by central limit theorem and (2) in the supplementary material Liu (2014), $\mathbb{P}(|T_i| \geq G^{-1}(m^{-\theta^2/2+\epsilon})) \rightarrow 1$ uniformly for $i \in \mathcal{H}_1$. Hence

$$\frac{\sum_{i \in \mathcal{H}_1} I\{p_i \leq m^{-\theta^2/2+\epsilon}\}}{m_1} \rightarrow 1$$

in probability as $m \rightarrow \infty$. By $\theta > \sqrt{2(1 - \beta + \epsilon)}$, we have $m^{1-\theta^2/2+\epsilon} = o(m_1)$, and hence $\hat{t}_{BH} \geq m^{-\theta^2/2+\epsilon}$ with probability tending to one. This implies that

$$\frac{\sum_{i \in \mathcal{H}_1} I\{p_i \leq \hat{t}_{BH}\}}{m_1} \rightarrow 1$$

in probability as $m \rightarrow \infty$. Suppose that $\theta \geq \sqrt{2(1 + \epsilon)}$. Then we have $\mathbb{P}(|T_i| \geq \sqrt{2 \log m}) \rightarrow 1$ uniformly for $i \in \mathcal{H}_1$. This yields that

$$\frac{\sum_{i \in \mathcal{H}_1} I\{p_i \leq G(\sqrt{2 \log m})\}}{m_1} \rightarrow 1$$

in probability as $m \rightarrow \infty$. By the definition of \hat{t}_{BH} , we have $\hat{t}_{BH} \geq \alpha/m \geq G(\sqrt{2 \log m})$ when m is large, which implies that

$$\frac{\sum_{i \in \mathcal{H}_1} I\{p_i \leq \hat{t}_{BH}\}}{m_1} \rightarrow 1$$

in probability as $m \rightarrow \infty$. The proof of the theorem is complete. \blacksquare

6.4 Proof of Theorem 3.4

We only need to prove the theorem when $\gamma < 1$. Let τ_m satisfy

$$\sum_{i \in \mathcal{H}'_0} \mathbb{P}(|N(0, 1) + h_i| \geq \tau_m \sqrt{\log m}) = m^{\beta^*},$$

where $\beta^* = \beta + \min(1 - \beta, \theta^2/4)$ and

$$\mathcal{H}'_0 = \left\{ i \in \mathcal{H}_0 : \left| \frac{n_1}{\sigma_{i,1}^2(1 + \frac{n_2\sigma_{i,1}^2}{n_1\sigma_{i,2}^2})} \mu_{i,1} + \frac{n_2\sigma_{i,1}^2}{n_1\sigma_{i,2}^2} \mu_{i,2} \right| < h \sqrt{\log m} \right\}.$$

We have $\tau_m \leq h + \sqrt{2(1 - \beta^*)} + \varepsilon$ for any $\varepsilon > 0$ when m is large. Since $h \leq 2$, there exists an k^* such that $k^*/N \leq \tau_m \leq (k^* + 1)/N$. Set

$$\sum_{i \in \mathcal{H}'_0} \mathbb{P}(|N(0, 1) + h_i| \geq (k^*/N) \sqrt{\log m}) = m^{q_m},$$

where, by the tail probability of normal distribution, q_m satisfies $|q_m - \beta^*| < (\tau_m + h)/N + 1/N^2 \leq 7/N$. Since $N \geq 10/\min(1 - \beta, \theta^2/4)$, we have $q_m \geq \beta + \epsilon$ for some $\epsilon > 0$. By Lemma 6.1 and the proof of Lemma 6.3, we can show that

$$\frac{\sum_{i \in \mathcal{H}'_0} I\{|S_i| \geq (k^*/N) \sqrt{\log m}\}}{m^{q_m}} \rightarrow 1$$

in probability. Hence $P(\hat{m}_{1,\lambda^*}^o \geq m^{q_m}/2) \rightarrow 1$ with $\lambda = (k^*/N)\sqrt{\log m}$ and $\hat{m}_{1,\lambda^*}/\hat{m}_{1,\lambda^*}^o \rightarrow 1$ in probability. Put

$$\mathcal{H}'_1 = \left\{ i \in \mathcal{H}_1 : \sqrt{\frac{n_1}{\sigma_{i,1}^2(1 + \frac{n_2\sigma_{i,1}^2}{n_1\sigma_{i,2}^2})}} \left| \mu_{i,1} + \frac{n_2\sigma_{i,1}^2}{n_1\sigma_{i,2}^2} \mu_{i,2} \right| \geq \kappa \sqrt{\log m} \right\}.$$

We have $\kappa > \tau_m + \epsilon \geq k^*/N + \epsilon$ for some $\epsilon > 0$. Let $x_m = (\theta - \epsilon_1)\sqrt{\log m}$ for some $\epsilon_1 > 0$ such that $\theta - \epsilon_1 > \sqrt{\max(0, 2\gamma - 2\beta)}$. It is easy to show that

$$P(|S_i| \geq (k^*/N)\sqrt{\log m}) \rightarrow 1 \quad \text{and} \quad P(|T_i| \geq x_m) \rightarrow 1$$

uniformly in $i \in \mathcal{H}'_1$. Hence

$$P(|S_i| \geq (k^*/N)\sqrt{\log m}, |T_i| \geq x_m) \rightarrow 1$$

uniformly in $i \in \mathcal{H}'_1$. By Markov's inequality,

$$\frac{\sum_{i \in \mathcal{H}'_1} I\{|S_i| \geq \lambda^*, |T_i| \geq x_m\}}{|\mathcal{H}'_1|} \rightarrow 1$$

in probability. Since $N \geq 10/\min(1 - \beta, \theta^2/4)$, we have $q_m \leq \beta^* + 7/N \leq \beta + 1.7 \min(1 - \beta, \theta^2/4)$. Also, $P(\hat{m}_{1,\lambda^*} \leq m^\gamma + 2m^{q_m}) \rightarrow 1$. By taking ϵ_1 in x_m sufficiently small, we have $\hat{m}_{1,\lambda^*}G(x_m) = o(|\mathcal{H}'_1|)$ as $|\mathcal{H}'_1| \geq \rho m^\beta$. Hence $P(\hat{t}_{1,\lambda^*} \leq x_m) \rightarrow 1$. So $P(|\mathcal{R}_{11,\lambda^*}| \geq (1 - \varepsilon)\rho m^\beta) \rightarrow 1$ for any $\varepsilon > 0$, where

$$\mathcal{R}_{11,\lambda^*} = \left\{ i \in \mathcal{H}_1 : I\{|S_i| \geq \lambda^*, |T_i| \geq \hat{t}_{1,\lambda^*}\} = 1 \right\}.$$

By the definition of $\hat{t}_{1,\lambda}$,

$$\hat{m}_{1,\lambda^*}G(\hat{t}_{1,\lambda^*}) = \alpha \max(1, \sum_{i=1}^m I\{|S_i| \geq \lambda^*, |T_i| \geq \hat{t}_{1,\lambda^*}\}).$$

By (10), $FDP_{1,\lambda^*}(\hat{t}_{1,\lambda^*}) \rightarrow \alpha$ in probability. So $P(|\mathcal{R}_{1,\lambda^*}| \geq \rho(1 - \alpha + \varepsilon)^{-1}m^\beta) \rightarrow 1$ for any $\varepsilon > 0$, where

$$\mathcal{R}_{1,\lambda^*} = \left\{ 1 \leq i \leq m : I\{|S_i| \geq \lambda^*, |T_i| \geq \hat{t}_{1,\lambda^*}\} = 1 \right\}.$$

Since $|\mathcal{R}_{\hat{\lambda}}| \geq |\mathcal{R}_{\lambda^*}|$, it follows that

$$P(|\mathcal{R}_{\hat{\lambda}}| \geq \rho(1 - \alpha + \varepsilon)^{-1}m^\beta) \rightarrow 1.$$

By Theorem 3.1, $P(FDP \leq \alpha + \varepsilon) \rightarrow 1$ for any $\varepsilon > 0$. This implies that $P(\text{power}_{US} \geq \rho - \varepsilon) \rightarrow 1$ for any $\varepsilon > 0$. ■

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